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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,888	01/04/2007	Rolando Pajon Feyt	976-33 PCT/US	5857

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HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
02/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,888	FEYT ET AL.	
	Examiner	Art Unit	
	Oluwatosin Ogunbiyi	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 May 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment to the claims filed12/28/07 is entered into the record. Claims 1-31 are cancelled. Claims 32-46 are pending in the application and are under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

New corrected drawings are required in this application because figures 3 and 6 are not legible. There are no visible protein bands in the figures.

The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

The specification contains non-English language. See p. 12 lines 25-26.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See p. 12 line 17, p. 13 line 5, and p. 16 lines

19-34. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Information Disclosure Statement

The information disclosure statement filed 9/5/06 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicants' election of Group I, claims 1-2,4-23,27 and 28 in the lack of unity filed 10/31/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicants have now cancelled claims 1-31 and claims 32-46 are now pending and under examination.

Claim Rejections - 35 USC § 101

Claims 32-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The claims are drawn to a method of preventing an infection caused by bacteria from a *Neisseria* genus in a human in need thereof and a method of treating an infection caused by bacteria from a *Neisseria* genus comprising administering to said human an

effective amount of a recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4.

The prevention of a bacterial infection is not credible. The broadest reasonable interpretation of the term infection merely requires that one microorganism gain entry into the cells of a host. Prophylactic/preventative treatments e.g. vaccines for many infections do not prevent infection i.e. the entry of at least one microorganism but instead kill the organism once it infects tissues or cells thereby eliminating the infection or reducing microorganism burden, thus reducing or eliminating any disease caused by the infection . Such treatments do not prevent the organism from infecting in the first place. Prevention of infection by a bacterium in general is a very high bar because the vaccine must prevent at least one bacterium from infecting a cell. Also, prevention of infection is different from prevention of disease caused by an infection as prevention of disease is prevention of symptoms due to an infection while preventing infection is inhibition of the infectious organism from invading or entering, for example, the human body, tissue, cells in the first place. Furthermore, the invention requires prevention of infection caused a *Neisseria* genus. The *Neisseria* genus comprises some of the following species *meningitidis*, *lactamica, cinerea, gonorrhoeae, flava and elongata* (Stern et al. US 5378606, 1995. See under description). *Neisseria* genus also comprises different serogroups of each species. For example, *Neisseria meningitidis* has 12 serogroups (Fraser et al WO 99/57280, 1999, p.1 last paragraph). Therefore, the scope of the claims is extremely broad. The invention is drawn to the use of a single protein - SEQ ID NO: 4 which is disclosed as a *Neisseria meningitidis* serogroup B

protein to prevent infection due to all Neisseria bacteria. The instant specification does not provide any evidence for prevention of an infection i.e. prevention of at least one single *Neisseria* bacterium from infecting a human. In figure 10 of the instant specification, antibodies specific for SEQ ID NO: 4 did not prevent infection of bacteria in rats. Clearly figures 10, shows that rats immunized with antibodies are still infected albeit at reduced titers. As an example, in the case of *Neisseria gonorrhoeae*, vaccines are not yet available for treating gonorrhea infection (Moxon et al. British Medical Bulletin 2002; 62: 45-48 see abstract; Blake et al. Trends in Microbiology 3:469-474) and the art does not teach a protein vaccine to prevent a *Neisseria gonorrhoeae* infection. The specification has not given guidance on how to prevent infection caused by any *Neisseria* bacteria in an animal model or in humans and it would be reasonable to conclude that the utility of the instant claims would not be credible utility based on the evidence of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment (reducing bacteria titers) of *Neisseria meningitidis* serogroup B infection in rats, does not reasonably provide enablement for treatment of infections caused by *Neisseria* in humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted

factual considerations. *In re Wands*,858 F.2d at 737, 8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection are discussed below.

The nature of the invention is treating an infection caused by bacteria from a *Neisseria* genus. The invention is to be practiced in humans by administering an effective amount of a single recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4. The invention requires treatment of infection caused by a *Neisseria* genus. The scope of *Neisseria* genus is extremely broad and comprises some of the following species *meningitidis*, *lactamica, cinerea, gonorrhoeae, flava and elongata* (Stern et al. US 5378606, 1995. See under description) and the different serogroups of each species. For example, *Neisseria meningitidis* has 12 serogroups (Fraser et al WO 99/57280, 1999, p.1 last paragraph). The nature of the invention is highly complex as it involves heterologous protection afforded by a single protein antigen across all *Neisseria* species and all *Neisseria* serogroups.

The specification teaches that protein NMB0928 (SEQ ID NO:4) is a *Neisseria meningitidis* serogroup B protein with 96% sequence identity with a protein from *Neisseria* gonorrhoeae (p. 16 example 5 and fig. 8). The specification is silent as to whether SEQ ID NO: 4 shares sequence identity with proteins from other *Neisseria* species. The specification teaches that SEQ ID NO: 4 induce an immune response when administered to mice (p. 17 example 6). The specification also teaches that immune sera obtained from said immunized mice reduced bacterial counts in rats

challenged with bacteria (strain CU385) one hour after administering said sera (p.17 example 7, and see figure 10). The specification does not teach whether said immune sera reduces bacterial counts in rats challenged with the other eleven *Neisseria meningitidis* serogroups two of which are serogroup A and C and other *Neisseria* species as listed above.

The art teaches that it remains unknown whether titers of antigroup B meningococcal bactericidal antibody correlate with protection from disease. Animal models of *Neisseria meningitidis* serogroup B infection including infant rat model and rabbit model of bacteremia have been employed but it is not established how animal data relates to protection from disease in humans. The main problem with these models is the validity of extrapolating results to human disease. For, serogroup B vaccines, there is no consensus about the correlation between vaccine efficacy and a particular in vitro measure and further work is needed. The search for the universally cross-protective meningococcal antigen or vaccine has yet to be successful. See reviews by Bethell et al, 2002, Expert Rev. Vaccines 1 (1), 75-84, p. 77 left column and Riddell and Buttery , 2001 Exp. Opin. Biol. Ther. 1 (3):385-399, p. 391 left column, p. 395 left column under expert opinion).

In view of the art teachings above, it is unpredictable whether SEQ ID NO:4 (a *Neisseria meningitidis* serogroup B protein) will be efficacious in treating any *Neisseria* infection in a human because the art teaches that there is a problem with extrapolating results from animal models to humans. Furthermore, it is unpredictable whether, the instant serogroup B protein will be efficacious in treating bacterial infections caused by

the other eleven *Neisseria meningitidis* serogroups as the art teaches that there is no single protein candidate which would protect all serogroups and strains of meningococcus (Riddell and Buttery et al, p. 395 left column under expert opinion) and the instant specification does not provide any evidence that the instant protein is cross protective across all meningococcus serogroups and strains. In addition, it is unpredictable from the instant specification teachings that the instant protein treats infection caused by other *Neisseria* species. In the case of *Neisseria gonorrhoeae*, a vaccine is not yet available for treating gonorrhea infection (Moxon et al. British Medical Bulletin 2002; 62: 45-48 see abstract; Blake et al. Trends in Microbiology 3:469-474).

The fact that the instant protein shares > 90% sequence identity with sequences in meningitidis serogroups A and C and *Neisseria gonorrhoeae* does not predict the cross protectiveness of the instant protein in treating infections caused by these other *Neisseria*. As mentioned above, in the *Neisseria* vaccine art there is yet no protein candidate which would protect all serogroups and strains of meningococcus and other *Neisseria* species and the instant specification does not provide evidence for cross protection. For such an unpredictable art i.e. treatment of infections caused by bacteria from all *Neisseria* genus in a human using a single protein more guidance and a working example is need because as set forth above the art teaches that there is no single protein candidate which would treat infections caused by all serogroups and strains of *Neisseria meningococcus* in humans (Riddell and Buttery et al, 2001) and there is no evidence that a single protein would treat infection due to the broad genus of *Neisseria* and most importantly the art teaches that it is not established how animal

data obtained from experiments with animal models of *Neisseria meningitidis* serogroup B infection relates to protection from disease in humans because there is an issue with extrapolating results from said models to humans (Bethell et al, 2002, Expert and Riddell and Buttery , 2001).

Therefore, in view of the above factors it would require undue experimentation on the part of the skilled artisan to use the invention to treat all *Neisseria* genus infections in humans with a single *Neisseria meningitidis* serogroup B protein as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-36, 39-40, and 42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Fraser et al. WO 99/57280, November 1999.

The claims are drawn to a method of preventing an infection caused by bacteria from a *Neisseria* genus in a human in need thereof and a method of treating an infection

caused by bacteria from a *Neisseria* genus comprising administering to the human an effective amount of a recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4.

Fraser teaches a method of treating and preventing an infection due to *Neisseria* bacteria such (p. 7 4th full paragraph) in a human (p. 34 2nd full paragraph) by administering to said human an effective amount (p. 36 2nd full paragraph) of a protein comprising an amino acid sequence that is 100% identical to SEQ ID NO: 4. See sequence alignment (provided in previous office action dated 10/31/07) and SEQ ID NO: 1522 on p. 798 of Fraser et al. Fraser et al teaches said method wherein the bacteria is *Neisseria meningitidis* and wherein the bacteria is *Neisseria gonorrhoeae*. Fraser et al teaches said method comprising administering pharmaceutical compositions of said protein and a pharmaceutically acceptable carrier (p. 34 see under vaccines) wherein said pharmaceutical composition further comprises a polysaccharide antigen (p. 33 4th full paragraph); wherein said composition further comprises inactivated virus particles (inactivated microorganism, p. 33 4th full paragraph); wherein in said pharmaceutical composition further comprises a peptide antigen (p. 35 last paragraph); wherein in said pharmaceutical composition further comprises macrophage colony stimulating factor (growth factor, p. 35 2nd full paragraph); wherein said pharmaceutical composition is administered parenterally (p. 36 2nd to the last paragraph) and wherein said pharmaceutical composition is administered mucosally (via oral route, p. 36 2nd to the last paragraph).

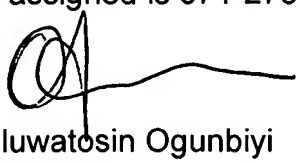
Status of the Claims

Claims 32-46 are rejected. No claims allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Oluwatosin Ogunbiyi
Examiner
Art Unit 1645